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(54) Title: INHIBITION OF SYSTEMIC INFECTIONS IN HUMANS AND VERTEBRATES BY DIETARY FIBERS

(57) Abstract: The use of a dietary fiber or mixture of dietary fibers for the manufacture of a composition, such as a pharmaceutical composition, a functional food or a functional feed, for the prevention, the inhibition and/or treatment of systemic infections in humans and in vertebrates caused by pathogenic bacteria is disclosed. A method for preventing and/or inhibiting the systemic growth of pathogenic bacteria in humans and vertebrates, and a method for the prevention, the inhibition and/or the treatment of systemic infections in humans and in vertebrates caused by pathogenic bacteria, comprising administration to said beings a composition containing an effective amount of a dietary fiber or mixture of dietary fibers, are also disclosed. The dietary fiber is preferably a fructan, typically inulin and/or oligofructose, most preferably chicory inulin with an average degree of polymerisation *DP* of at least 20. The composition and methods are useful for the prevention, inhibition and/or treatment of systemic infections in fish, particularly during cultivation in fish farms.

INHIBITION OF SYSTEMIC INFECTIONS IN HUMANS AND VERTEBRATES BY DIETARY FIBERS

Field of the invention

The present invention relates to the use of a dietary fiber, particularly a fructan, for the manufacture of a composition for preventing and/or inhibiting the systemic growth of pathogenic bacteria in humans and vertebrates. The present invention also relates to a method for preventing and/or inhibiting the systemic growth of pathogenic bacteria in humans and vertebrates, as well as to a method for the prevention, inhibition and/or treatment of systemic infections in humans and vertebrates by administration of a composition containing a dietary fiber, particularly a fructan.

Background and prior art

Dietary fiber is a general term that is used to describe food ingredients that are resistant to hydrolysis by the digestive secretions of humans and vertebrates (referred to in short herein by the term resistant). Historically, dietary fibers have been considered to primarily consist of lignin, cellulose, hemicellulose or pectin. However, recent interest has focused on other dietary fibers such as *e.g.* resistant starch and resistant fructans, including levan, inulin and oligosaccharides.

The sources of dietary fiber vary widely and may include trees (cellulose), beet pulp from sugar beets, and extracts from plants, plant parts and fruits (*e.g.* gum arabic, fructans, including levan from Phleum pratense, and inulin and fructo-oligosaccharide, also named oligofructose, from roots of chicory and from tubers of Dahlia and Jerusalem artichoke; citrus pectin from fruits; carrageenan from seaweed; and husks from nuts (*e.g.* peanut hulls). Although resistant oligosaccharides have traditionally not been considered as dietary fibers, they do meet the necessary criteria, and are now generally accepted as such. Resistant oligosaccharides and polysaccharides can also originate from bacterial activity (*e.g.* fructo-oligosaccharide, levan and inulin) and can also be obtained by enzymatic synthesis, *e.g.* fructo-oligosaccharide from sucrose. Resistant oligosaccharides can be obtained too by partial hydrolysis of resistant

polysaccharides, for example fructo-oligosaccharide by partial, acidic or enzymatic hydrolysis of fructans. The terms fructo-oligosaccharide and oligofructose are used herein interchangeably.

Fructans, i.e. levan and inulin commonly occur as a polydisperse mixture of chains of carbohydrates which consist mostly of fructose units and in which fructosyl-fructose linkages constitute the majority of the linkages. Fructo-oligosaccharide or oligofructose, which is in fact a fructan composed of molecules with less than 10 saccharide units, can be obtained by extraction from plant material, by partial hydrolysis, either acidic hydrolysis or enzymatic hydrolysis, of fructans, particularly inulin, as well as by enzymatic synthesis from sucrose. All these types of fructans are embraced herein by the term fructan.

Fructans, including levan, inulin and oligofructose, are well known in the art and are considered as dietary fibers. Levan consists of chains of fructose units which are mostly or exclusively connected to each other by ß(2-6) linkages. A terminal glucose unit may be present or not. Inulin consists of chains of fructose units which are mostly or exclusively connected to each other by ß(2-1) linkages. Most of the inulin chains terminate in one glucose unit but the presence of said glucose unit is not necessary. Levan mostly occurs as branched fructose chains, whereas inulin is composed of linear chains of fructose units but it may also occur as chains of fructose units which are branched to a larger or lesser extent. All said fructans, i.e. levan, inulin and oligofructose, are suitable in the present invention.

Inulin occurs at concentrations of about 10 to 20 % on fresh weight in chicory, dahlia tubers and Jerusalem artichoke, from which it can be isolated at industrial scale, purified, and optionally refined to remove impurities and undesired fractions of carbohydrates, according to known techniques.

Inulin can be represented by the general formulae GF_n and F_m wherein G represents a glucose unit, F represents a fructose unit, n represents the number of fructose units linked to the terminal glucose unit,

and m represents the number of fructose units linked to each other in the carbohydrate chain. The number of saccharide units (fructose and glucose units) in one fructan molecule, *i.e.* the values n+1 and m in the above formulae, are commonly referred to as the degree of polymerisation, represented as (DP). A further feature of inulin is the (number) average degree of polymerisation, represented by ($\overline{DP}$), which is the mean number of saccharide units per polysaccharide (inulin) molecule.

Inulin from chicory is commercially available as RAFTILINE® from ORAFTI, (Tienen, Belgium), in various grades such as, for example, ST (which has a ($\overline{DP}$) of about 10 and contains in total about 8 % by weight glucose, fructose and sucrose), LS (which has a ($\overline{DP}$) of about 10 but which contains in total less than 1 % by weight glucose, fructose and sucrose), and HP (which has a ($\overline{DP}$) of ≥ 23, commonly of about 25, and contains in total less than 1 % by weight of glucose, fructose and sucrose).

Fructo-oligosaccharide (oligofructose) consists of chains of less than 10 fructose units which are mostly or exclusively connected to each other by ß(2-6) linkages or ß(2-1) linkages, and a terminal glucose unit may be present.

Oligofructose is commercially available, for example as RAFTILOSE® from ORAFTI, (Tienen, Belgium), in various grades such as, for example, RAFTILOSE® P95 which contains about 95 % by weight oligofructose, composed of chains with a degree of polymerisation ranging from 2 to about 7, typically with a ($\overline{DP}$) of 3.5 to 4.5, and containing about 5 % by weight in total of glucose, fructose and sucrose.

Dietary fibers can be classified based on their solubility in water and can also be classified on whether or not the dietary fiber can be used as energy source by bacteria of the gastro-intestinal tract whereby the dietary fiber is metabolised (fermented). Fibers that can be used by gastro-intestinal bacteria are considered to be fermentable. The terms fermentable fibers and dietary fibers are used interchangeably herein.

Dietary fibers appear to have relevance in improving human and animal health. The gastro-intestinal tract of humans and vertebrates contains many species of bacteria, some of which that are commonly present are considered as beneficial, whereas others, which typically are present in the gastro-intestinal tract in case of a bacterial infection, are considered as pathogens. The term pathogenic bacteria includes herein typically pathogenic bacteria as well as putrefactive bacteria.

Beneficial bacteria include the abilities of the production of lactic acid, other short chain fatty acids, metabolites and other chemical compounds, that are known to have beneficial effects on certain bodily functions and that suppress the growth of pathogenic bacteria species in the gastro-intestinal tract, a process called inhibition. Promotion of the growth of said beneficial bacteria, such as bifidobacteria and lactobacilli, by intake of dietary fibers, particularly inulin and resistant oligosaccharides such as *e.g.* oligofructose, thus results in various beneficial effects for the host, including *e.g.* in humans increase of stool weight and stool frequency with reduction of constipation, reducing effects of glycemic response, effects on blood cholesterol and on HDL/LDL ratio, and effects on serum lipids. Further effects include immuno-modulating effects resulting *i.a.* in protective, inhibiting and/or curative effects on cancer in humans and mammals, particularly on breast and on colon cancer. Beneficial bacteria of the gastro-intestinal tract typically include bacteria of the genus *Bifidobacterium* (Bifidus) and *Lactobacillus*.

Pathogenic bacteria may cause to the host various diseases and dysfunctions, including diarrhoea and infectious diseases, such as entero-colitis, gastro-intestinal ulcers and Crohn's disease.

It is known that beneficial bacteria, particularly those of the genus *Bifidobacterium* and *Lactobacillus*, have the capacity to ferment dietary fibers, typically fructans and resistant oligosaccharides, more effectively than pathogenic intestinal bacteria. Thus the intake of dietary fibers, particularly of fructans and/or resistant oligosaccharides, increases the density of lactic

acid producing bacteria in the gastro-intestinal tract and reduces the number of undesirable Enterobacteriaceae. The latter include most pathogens such as *e.g.* bacteria of the genus *Clostridia, Bacteroides, Listeria, Candida* and *Salmonella.* Accordingly, intake of dietary fibers such as fructans and/or oligofructose can be used to selectively stimulate the growth of beneficial bacteria in the gastro-intestinal tract. The improvement of the ratio beneficial / pathogenic bacteria in turn results in beneficial health effects for the host.

To prevent, control and/or remedy disorders and diseases of the gastro-intestinal tract of humans and vertebrates caused directly or indirectly by pathogenic bacteria, several approaches are used today. A first approach is the intake of antibiotics which can selectively remove a target genus of bacteria. A second approach is the intake of probiotics, which are viable, beneficial bacteria, such as bifidobacteria and lactobacilli, enabling to alter the composition and, accordingly, the metabolism of the gastro-intestinal flora, and thus to beneficially affect the host's health. A third approach involves the intake of prebiotics, i.e. dietary fibers, which increases the ratio beneficial/pathogenic bacteria in the gastro-intestinal tract with a concurrent reduction of undesired, pathogenic and putrefactive bacteria, resulting in beneficial health effects for the host, such as *e.g.* permitting faster recovery of mucosal mass and digestive capacities, and the inhibition and/or relieve of gastro-intestinal dysfunctions and diseases. In a fourth approach lectins, certain monosaccharides such as *e.g.* mannose, and certain organic acids such as mono-, di- and tricarboxylic acids, have also been used to selectively decrease the density of some pathogenic bacteria.

Gastro-intestinal dysfunctions and diseases, such as severe diarrhoea and gastro-enteritis often lead to disruption of the mucosal barrier which increases the risk of translocation of bacteria from the gastro-intestinal tract to the mesenteric lymph nodes and to the blood stream, often causing subsequent sepsis in the host. However, penetration of bacteria, into the bloodstream or another bodily fluid may occur not only through a disrupted

mucosa of the gastro-intestinal tract, but via any disrupted, weakened or malfunctioning barrier, such as *e.g.* the gill or skin of fish, and may subsequently cause sepsis in the host. Sepsis caused by bacteria that passed a host's barrier is conventionally and hereinafter named a systemic infection.

Nowadays, said sepsis is commonly inhibited and treated by means of antibiotics which are administered to the infected host. Besides, in order to control the growth of pathogenic bacteria and infection of the gastro-intestinal tract, as well as to prevent subsequent systemic infection by said pathogenic bacteria in vertebrates, often antibiotics are added to feed.

However, there is a growing concern about the use of antibiotics because of the development of bacterial strains that are resistant to antibiotics and the potential impact they have on the environment. Another detriment of the treatment with some antibiotics is the disruption of the normal gastro-intestinal bacterial flora.

Accordingly, there is an ongoing search for compounds and methods for the prevention, inhibition and treatment of systemic bacterial infections which are free of one or more disadvantages presented by the compounds and methods which are currently used in this respect.

Summary of the invention

During studies of the effects of the intake of fermentable fibers on humans and vertebrates, the inventors have found that the oral administration (including administration via tube feeding) and/or rectal administration of dietary fibers, in particular inulin and oligofructose, does not only effect the gastro-intestinal flora by stimulating the growth of beneficial bacteria and by improving the ratio beneficial / pathogenic bacteria, but, surprisingly, also has beneficial effects on the host's response to systemic infections by pathogenic bacteria.

Said findings lead to the present invention, which in one aspect, relates to the use of a dietary fiber or mixture of dietary fibers for the manufacture of a composition, such as *e.g.* a pharmaceutical composition or

a functional food composition or a functional feed composition, for the prevention, the inhibition and/or the treatment of systemic infections in humans and in vertebrates caused by pathogenic bacteria. The said composition can be manufactured in accordance with conventional techniques.

In a second aspect, the present invention relates to a method for preventing and/or inhibiting the systemic growth of pathogenic bacteria in humans and vertebrates, and provides a method for the prevention, the inhibition and/or the treatment of systemic infections in humans and in vertebrates caused by pathogenic bacteria, comprising administration to a human or a vertebrate, orally, through tube feeding or rectally, of a composition, being a functional food composition, a functional feed composition or a pharmaceutical composition, containing an effective amount of a dietary fiber or mixture of dietary fibers.

Brief description of the drawings

Figure 1: shows data from a mouse model. Survival over a 14 day period is shown for mice systemically infected with *Listeria monocytogenes* which were fed a diet including (a) cellulose, (b) oligofructose and (c) inulin.

Figure 2: shows data from a mouse model. Survival over a 14 day period is shown for mice systemically infected with *Salmonella typhimuriun* which were fed a diet including (a) cellulose, (b) oligofructose and (c) inulin.

Detailed description of the invention

In accordance with the present invention, the term dietary fiber, also named herein interchangeably fermentable fiber, indicates an edible compound, including lignin, an oligomeric carbohydrate and a polymeric carbohydrate, that is resistant to hydrolysis by the enzymes of the digestive tract of humans and vertebrates. The term dietary fiber includes lignin, cellulose, hemicellulose, pectin, gums such as *e.g.* arabic gum, carrageenan, waxes, and resistant oligosaccharides, such as *e.g.* oligofructose (term

interchangeably used with fructo-oligosaccharide), and resistant polysaccharides, such as *e.g.* resistant starch and fructans, including levan and inulin. Preferred dietary fibers include inulin, oligofructose and mixtures thereof. More preferred fibers include chicory inulin with a ($\overline{DP}$) of at least 20; most preferred are chicory inulin with a ($\overline{DP}$) of at least 25.

According to the present invention, systemic infection caused by pathogenic bacteria in humans and vertebrates can be prevented, inhibited and/or treated by the oral intake and/or rectal intake of dietary fibers.

The term oral administration/oral intake herein commonly includes administration through tube feeding.

Said fibers can be present in a pharmaceutical composition (medicament) together with pharmaceutically acceptable excipients, optionally in the presence of one or more additionally, physiologically active substances. Said medicament commonly occurs in a conventional galenic form that ensures it is suitable for oral administration, for tube feeding or for rectal administration, such as *i.a.* tablets, lozenges, capsules, syrups, suspensions, emulsions, solutions and suppositories.

Said fibers can also be present as the functional ingredient in a functional food composition or a functional feed composition, which is a food or feed product that may provide a health benefit beyond the traditional nutrients it contains.

Preferably an effective amount of the dietary fibers, in the form of a suitable composition, is administered daily, either in a single dose form or in two or more daily doses. The total daily amount of dietary fibers may widely vary and depend *i.a.* of the nature of the fiber or fiber mixture, the host, and the effect aimed at *e.g.* an preventive, an inhibitory or a treatment effect. The optimal daily dose commonly corresponds to the maximal amount that the host can consume without suffering from significant undesirable side effects commonly concurring with the intake of too large amounts of dietary fibers, such as flatulence and diarrhoea. The optimal dose can be found in the prior art literature and/or can be determined by the

skilled person through routine experiments. For human adults the daily dose of inulin and/or oligofructose generally ranges from 5 to 40 g/day, typically the optimal dose may range from 5 to 25 g/day.

When, in accordance with the present invention, a dietary fiber or mixture of two or more dietary fibers, particularly inulin and/or oligofructose, are administered to a human or a vertebrate, a significant preventive or inhibitory effect on the systemic growth of pathogenic bacteria has been observed.

Typical vertebrates which are quite sensitive to systemic infections caused by pathogenic bacteria include fish. As a result thereof high mortality rates, up to 80 % and even more, may occur in fish during cultivation in fish farms. Accordingly, the composition and method according to the present invention are very useful for the prevention and inhibition of systemic growth of pathogenic bacteria in fish, and the prevention, the inhibition and/or the treatment of systemic infections in fish, such as *e.g.* salmon, sturgeon, catfish, turbot and carp, particularly during cultivation of the fish in fish farms. In a typical approach the fish is given feed consisting of or comprising a composition according to the invention containing a dietary fiber or mixture of dietary fibers, particularly including inulin and/or oligofructose.

Furthermore, dietary fibers are free of toxic effects on the host and do not generate resistant bacterial strains. Furthermore, the fibers are fermented by beneficial gastro-intestinal bacteria of the host with exertion of various beneficial effects as mentioned above, and thus they have no detrimental environmental effects. Besides, the dietary fibers are obtained in economically manner from renewable resources. Accordingly, the use of dietary fibers in accordance with the present invention for the prevention, inhibition and/or treatment of systemic infections in humans and vertebrates, present considerable advantages over prior art compounds such as antibiotics.

The invention is illustrated by the examples given below.

Example 1.

Example 1 relates to a systemic infection caused by *Listeria monocytogenes*, a typical pathogenic bacteria species of the *Listeria* family which may cause a disorder named listeriosis. In most serious cases, the manifestations of listeriosis include septicemia, meningitis (or meningoencephalitis), encephalitis and intrauterine or cervical infections in pregnant woman, which may result in spontaneous abortion or stillbirth. The onset of said disorders is usually preceded by influenza-like symptoms, including headache and persistent fever. Furthermore, gastro-intestinal disorder symptoms such as nausea, vomiting and diarrhoea may precede serious forms of listeriosis or may be the only symptoms expressed.

Listeriosis is clinically defined when the organism, *Listeria monocytogenes*, is isolated from blood, cerebrospinal fluid, or an otherwise normally sterile site such as *e.g.* the placenta. *Listeria monocytogenes* may invade the gastro-intestinal epithelium. Once the bacterium enters the host's monocytes, macrophages or polmymorphonuclear leucocytes, it is bloodborne (septicemic) and can grow. Its presence intracellularly in phagocytic cells also permits access to the brain and probably transplacental migration to the fetus in pregnant women. Nearly one out of four people seriously infected by *Listeria monocytogenes* may die.

The pathogenesis of *Listeria monocytogenes* is based on its ability to survive and multiply in phagocytic host cells.

Culture of *Listeria monocytogenes*.

Listeria monocytogenes of the virulent EGD strain (Erdenlig, Ainsworth and Austin, J. Food Protection, 63, 613-619, (2000)) were grown on blood agar plates at 37°C for 24 hours. The bacteria were harvested, suspended in 0.9 % saline, and washed twice by centrifugation (3,200 x g; 5 min). The sedimented bacteria were again suspended in 0.9 % sterile saline. The washed bacteria were propagated overnight in 37°C tryptose broth that was shaken. The

suspensions of growing bacteria were diluted to an optical density that corresponded with the desired concentration of 1 to 5 x 10^7 bacteria per ml. This was confirmed by plating aliquots on blood agar plates and enumerating the resulting colonies.

Infection of B6F3F1 mice with *Listeria monocytogenes.*

The propagated *Listeria monocytogenes* was given to 25 mice by injecting with 0.1 ml intraperitoneally (infective dose of 1–5 x10^6). The infective dose of bacteria was determined in preliminary studies that showed this dose of *Listeria monocytogenes* would result in 30 – 40 % mortality over a 14 day period.

Preparation of dietary supplement formulation.

All diets were prepared as pellets by Research Diets, Inc. (New Brunswick, NJ). The mice were fed diets based on the AIN 76 rodent diet, with 10% of the final weight as fiber (see Table 1, below). The control diet contained 10% of the insoluble and poorly fermented fiber cellulose (crystalline form). The experimental diets had the cellulose replaced entirely by oligofructose (RAFTILOSE® P95; ORAFTI, Belgium) or inulin (RAFTILINE® HP; ORAFTI, Belgium), which are fermented by the gastrointestinal bacteria and differ from one another with respect to the average degree of polymerisation ($\overline{DP}$) which is 4 and 25, respectively). The control and experimental diets were fed to the mice for 6 weeks before infection as presented in Table 1 below.

Table 1

Composition of the control and experimental diets[1] fed to the mice for 6 weeks before infection with *Listeria monocytogenes* (example 1) or *Salmonella typhimurium* (example 2). The diets continued to be fed to the mice for a 2 week period after infection.

Ingredient	gram
Casein, 30 mesh	200
DL Methionine	3
Corn Starch	150
Sucrose	450
Corn Oil	50
Salt Mix S10001[2]	35
Vitamin Mix V10001[3]	10
Choline Bitartrate	2
Fiber[4]	100

[1] Diets were formulated and prepared by Research Diets,Inc. (New Brunswick, NJ) and were based on the AIN 76 rodent diet.

[2] Composition of the salt mixture (amount in 35 g): calcium phosphate dibasic (Ca=5.2 g; P=4.0 g), magnesium oxide (Mg=0.5 g), potassium citrate (K=3.6 g), potassium sulfate (S=0.33 g), chromium potassium sulfate (Cr=2.0 mg), sodium chloride (Na=1.0 g; Cl=1.6 g), cupric carbonate (Cu=6.0 mg), potassium iodate (I=0.2 mg), ferric citrate (Fe=45 mg), manganous carbonate (Mn=59 mg), sodium selenite (Se=0.16 mg), zinc carbonate (Zn=29 mg), with sucrose as the remainder.

[3] Composition of the vitamin mixture (amount in 10 g): vitamin A palmitate (4,000 IU), vitamin D3 (1,000 IU), vitamin E acetate (50 IU), menadione sodium bisulfate (0.5 mg menadione), biotin (0.2 mg), cyanocobalamin (10 µg), folic acid (2 mg), nicotinic acid (30 mg), calcium pantothenate (16 mg), pyridoxine-HXI (7 mg), riboflavin (6 mg), thiamin HCl (6 mg), with sucrose as the remainder.

[4] The control diet contained cellulose as the only fiber source whereas the experimental diets had either 100 g of inulin or oligofructose.

The results of example 1 are shown in Figure 1. From the data presented in Figure 1 it clearly follows that mice fed a diet with cellulose, a non-fermentable fiber, experienced 28% mortality when infected systemically with *Listeria monocytogenes*. In contrast, mice fed the same diet, but with oligofructose mortality was less (12%) and inulin was even more effective with 0% mortality. These results demonstrate that a dietary supplement of oligofructose and inulin protects against systemic infections by a known pathogen.

Example 2

Example 2 relates to a systemic infection in mice caused by *Salmonella typhimurium*.

Many species of Salmonella exist, several of which cause foodborne illness. *Salmonella typhimurium* has been the species that accounts for most foodborne illnesses related to Salmonella bacteria. Recently another species, Salmonella enteritidis, has been associated with foodborne diseases resulting from consumption of contaminated undercooked eggs.

Disease is caused by the penetration and passage of Salmonella bacteria from gut lumen into epithelium of the small intestine where inflammation occurs.

Culture of *Salmonella typhimurium*.

Salmonella typhimurium (ATCC strain 14024) were passaged three times in B6F3F1 mice to assure virulence. Each time, *Salmonella typhimurium* were cultivated from spleens of dead mice. The resulting virulent strain was used as the representative bacterial pathogen. The virulent *Salmonella typhimurium* were grown on blood agar plates at 37°C for 24 hours. The bacteria were harvested, suspended in 0.9 % saline, and washed twice by centrifugation (3,200 x g; 5 min). The sedimented bacteria were suspended in 0.9 % sterile saline. The washed bacteria were propagated overnight in 37°C

CLAIMS

1. Use of a dietary fiber or mixture of dietary fibers for the manufacture of a composition for the prevention, the inhibition and/or the treatment of systemic infections in humans and in vertebrates caused by pathogenic bacteria.

2. Use according to claim 1 wherein the composition is selected from the group consisting of a pharmaceutical composition, a functional food, and a functional feed.

3. Use according to claim 1 or 2 wherein the composition is in a form which is suitable for administration, selected from the group consisting of oral administration, tube feeding, and rectal administration.

4. Use according to any of claims 1 to 3 wherein the dietary fiber or mixture of dietary fibers is selected from the group consisting of lignin, cellulose, hemicellulose, pectin, gums, arabic gum, carrageenan, waxes, resistant oligosaccharides, oligofructose, resistant polysaccharides, resistant starch and fructan.

5. Use according to claim 4 wherein the fiber is a fructan selected from the group consisting of inulin and oligofructose, or any mixture thereof.

6. Use according to claim 5 wherein the fiber is chicory inulin with an average degree of polymerisation ($\overline{DP}$) of at least 20.

7. Use according to claim 5 wherein the fiber is chicory inulin with an average degree of polymerisation ($\overline{DP}$) of at least 25.

8. Use according to any one of claims 1 to 7 wherein the vertebrate is fish and the composition is in a form for oral administration.

9. Use according to claim 8, wherein the fish is selected from the group consisting of salmon, sturgeon, catfish, turbot and carp.

10. Method for the prevention, inhibition and/or treatment of systemic infections in human or vertebrates caused by pathogenic bacteria comprising administering to said humans or vertebrates a composition containing an effective amount of a dietary fiber or mixture of dietary fibers.

11. Method according to claim 10 wherein the composition is administered orally, through tube feeding or rectally.

12. Method according to claim 10 wherein the composition is selected from the group consisting of a pharmaceutical composition, a functional food and a functional feed.

13. Method according to claim 10 wherein the dietary fiber or mixture of dietary fibers is selected from the group consisting of lignin, cellulose, hemicellulose, pectin, gums, arabic gum, carrageenan, waxes, resistant oligosaccharides, oligofructose, resistant polysaccharides, resistant starch and fructan.

14. Method according to claim 13 wherein the fiber is a fructan selected from the group consisting of inulin and oligofructose, or any mixture thereof.

15. Method according to claim 14 wherein the fiber is chicory inulin with an average degree of polymerisation ($\overline{DP}$) of at least 20.

16. Method according to claim 14 wherein the fiber is chicory inulin with an average degree of polymerisation ($\overline{DP}$) of at least 25.

17. Method according to claim 10 wherein the vertebrate is fish and the composition is administered orally.

18. Method according to claim 17, wherein the fish is selected from the group consisting of salmon, sturgeon, catfish, turbot and carp.

FIGURE 1

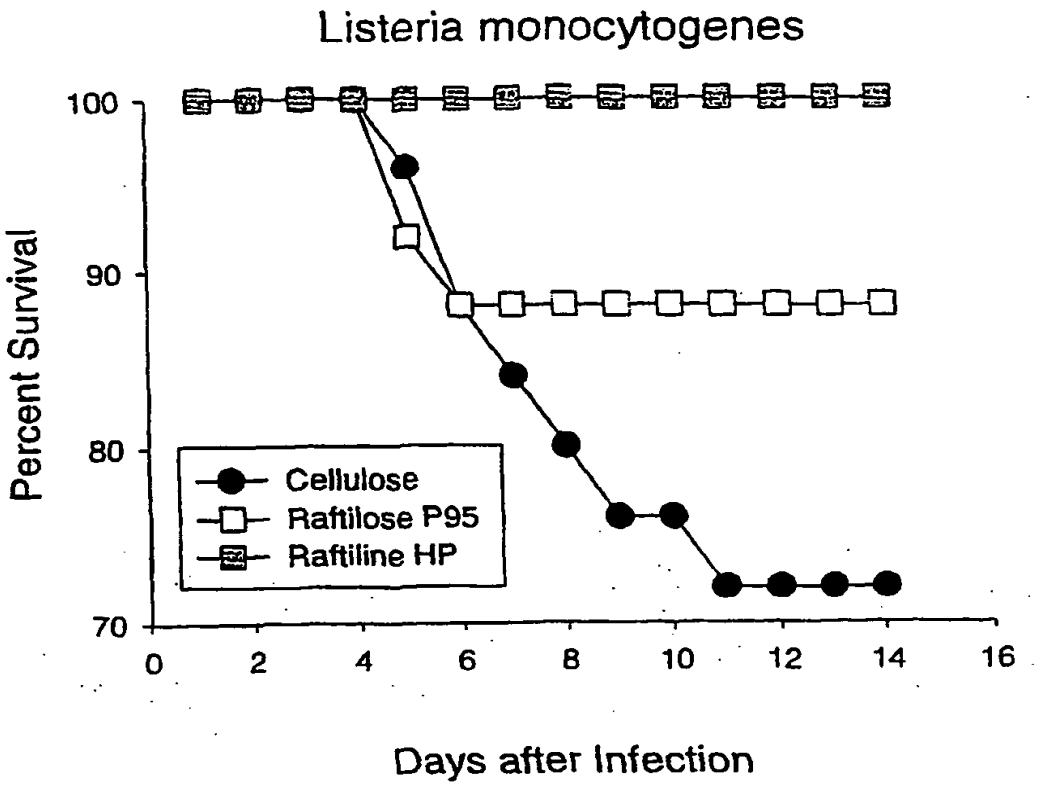
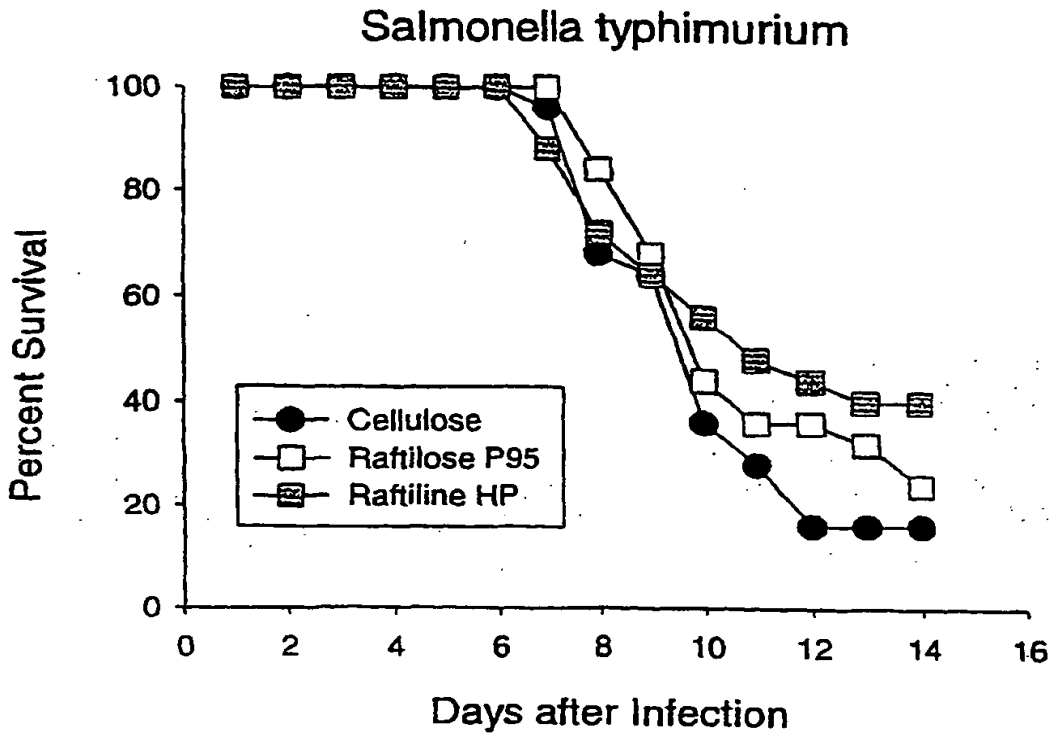

Listeria monocytogenes
Percent Survival
100
90
80
70
0
2
4
6
8
10
12
14
16
Cellulose
Raftilose P95
Raftiline HP
Days after Infection

FIGURE 2


Salmonella typhimurium
Percent Survival
100
80
60
40
20
0
0
2
4
6
8
10
12
14
16
Days after Infection
Cellulose
Raftilose P95
Raftiline HP